UNIVERSITY OF CALIFORNIA
Industry-University Cooperative Research Program
IUCRP WORKING PAPER SERIES

Assessing the Role of the University of California in the State's Biotechnology Economy: Heightened Impact Over Time

March 24, 2003
Working Paper 02-5

Cherisa Yarkin
Director, Economic Research

Andrew Murray
Principal Economic Analyst

A Working Paper of:
Economic Research and Assessment Unit
Industry-University Cooperative Research Program
University of California
2087 Addison Street 2nd floor
Berkeley, CA 94720-3340
URL:www.ucdiscoverygrant.org

Cherisa Yarkin, Ph.D., Director
cyarkin@uclink.berkeley.edu

Acknowledgements: A number of people contributed to this project, including Marco Thompson, president, San Diego Telecommunications Council; and Susanne Huttner who provided leadership and support. Research assistance was provided by Connie Choi, Cindy Lo, Christina Nagashima and Israel Moyston The views expressed are those of the authors, and not necessarily those of the University of California.

Cover: Design by TJ Tsuda.

Table of Contents

Appendices

Tables and Figures:

Assessing the Role of the University of California in the State's Biotechnology Economy:[i] Heightened Impact Over Time

The 2002 Report

Executive Summary

Scientific breakthroughs in biology, information sciences, physics and engineering have revolutionized the way products are developed, spurring the growth of entirely new industrial sectors. As this phenomenon has become widely recognized, economic development efforts at the local, state, and national levels have increasingly included investments in research and development, including basic academic research and graduate education.[ii] Although there is a broad consensus about the general benefits of such investment, understanding of the specific means by which such investments contribute to the economy remains incomplete. A diverse set of models, definitions, and datasets have been developed, but there remain gaps in our understanding of the channels through which benefits are created. [iii]

The University of California (UC) Industry-University Cooperative Research Program Economic Research and Assessment Initiative (the Project) aims to advance understanding of the role of public investments in academic science, at a time university-based fundamental research and advanced education is seen to be of increasing relevance to regional, national, and world economies. The Project explores new ways to assess the contributions made to the California economy by public R&D investment (through support for basic research and education). It focuses on the individuals who participate in that research and education as primary sources of contributions that help determine the course of economic growth. This approach complements and extends traditional assessment methodologies by moving beyond standard measures of publications and patents, and focusing on the people who generate the new knowledge these proxy measures are meant to reflect. It further enriches the standard view by identifying the multiple and varying roles that knowledge generators play over time.

This report describes a case study designed to assess the role of the University of California in the emergence and growth of commercial biotechnology in the state. The subset of biotechnology businesses examined comprises a substantial proportion of total commercial activity in the biotechnology sector. California is home to more than one third of U.S. public biotechnology companies, which in 2001 accounted for more than 47% of industry research and development

expenditures, and generated 53% of total US commercial biotechnology revenues.[iv] Commercial biotechnology in California provided more than 60,000 jobs that year, with average annual salaries of $75,000.[v] These patterns have remained strong over time, despite the rapid pace of change in the sector.[vi]

Building on the findings of the original biotechnology study undertaken in 1995-96, this reassessment of the state of the industry in 2002 illustrates the essential role publicly funded research and education have played, and continue to play, in the development of commercial biotechnology in California, which can be viewed as the field's center of origin and a continuing source of economic growth and innovation. The findings demonstrate that the University of California continues to be a driver on the commercial biotechnology economy.

- **1** in **4** U.S. public biotechnology firms is within 35 miles of a UC campus
- **1** in **6** U.S. public biotechnology firms was founded by UC scientists
- **1** in **3** California biotechnology firms was founded by UC scientists, including **5** of the world's **10** largest: Amgen, Genentech, Idec Pharmaceuticals, Applied Biosystems and Chiron[vii]

Work is underway to develop complementary case studies of other R&D intensive industry sectors to assess whether these results can be generalized beyond biotechnology. Early indications are that the framework and methodology we developed here provides useful insights into the emergence and growth of California's R&D intensive communications sector. Similar efforts in electronics manufacturing and new materials, and information technology for the life sciences have been launched, and when complete will provide a more extensive view of the economic impact of the University of California on the state's economy. The data collection effort undertaken for these studies is substantial, however; efforts are underway to find effective ways to streamline and simplify identification and collection of relevant information.

Introduction

The United States is at the forefront of a worldwide transition to a new economy of knowledge-driven economic development. Biotechnology, information and communications technologies have revolutionized the way products are developed, spurring the growth of entirely new industrial sectors. One area of particular policy interest is the role of academic research and training in creating science and technology (S&T)-based economic benefits. An increasing proportion of S&T research is being conducted at universities, [viii] but economists are still in the process of developing a complete understanding of how these investments generate economic returns.[ix] A wide array of models, definitions, and datasets has been developed, but there remain gaps in our understanding of the channels through which benefits are created, and how they might best be measured.[x]

The University of California (UC) Industry-University Cooperative Research Program Economic Research and Assessment Initiative (the Project) aims to advance understanding of the role of public investments in academic science, at a time university-based fundamental research and advanced education is seen to be of increasing relevance to regional, national, and world economies. The Project explores new ways to assess the contributions made to the California economy by public R&D investment (through support for basic research and education) over the past twenty years. It focuses on the individuals who participate in that research and education as primary sources of contributions that help determine the course of economic growth. This approach complements and extends traditional assessment methodologies by moving beyond standard measures of publications and patents, and focusing on the people who generate the new knowledge these proxy measures are meant to reflect. It further enriches the standard view by identifying the multiple and varying roles that knowledge generators play over time.

The Project was established in 1996, to amplify and extend the economic research on industry-university relationships begun in 1995 by the Critical Linkages Project (CLP). Launched by the UC Biotechnology Research and Education Program, the CLP developed a case study focused on the California economy and a particularly robust area of regional economic development: commercial biotechnology. Since its launch, the Project has undertaken to identify, document and develop a methodology for assessing and quantifying those contributions that accrue from publicly funded basic research and graduate education and from the relationships that develop between UC scientists and commercial biotechnology firms in California.

Why California?

California's preeminence in high technology industries stems from the application of unique scientific, educational, financial and business resources to the exploitation of new technological opportunities discovered through basic research. The biotechnology industry, one of the most innovative business sectors in the nation's economy, came into being in large part as a result of basic scientific research conducted at the University of California and Stanford University. The gene-splicing technique invented by Herb Boyer of UC San Francisco and Stanley Cohen of Stanford, for example, has provided the foundation for a rich array of entrepreneurial activity in biotechnology. In 1996, at the end of the patent period, 70 California biotechnology companies held licenses for the Cohen-Boyer technique, first patented in 1975.[xi]

While Stanford University has gained prominence for its role in commercial biotechnology, less is known about the scientific and educational contributions made by the University of California.[xii] Substantial investments have been made in research and education at the University over the past 35 years by both the federal government and the state of California. Public funds have supported capital projects, including laboratories and classroom facilities, as well as faculty salaries and other instructional services.[xiii] It is our contention that these long-standing investments have provided the foundation for California's vibrant knowledge-based, high technology economy.

The subset of biotechnology activity that we examine in this case study comprises a substantial proportion of total commercial activity in the biotechnology sector, as is shown in **Table 1**. California is home to 129 (38%) of the 342 U.S. public biotechnology companies in operation as of July 2002. These California firms spent more than $5.4 billion on R&D, which was 47% of the total US biotechnology industry research and development expenditures in 2001. They generated over $13.5 billion in revenues, or roughly 53% of total US commercial biotechnology revenues that year. Biotechnology companies in California provided more than 60,000 jobs in 2001, with average annual salaries of $71,000.[xiv] These patterns have remained strong over time, despite the rapid pace of change in the sector.[xv]

Table 1. The US Biotechnology Industry (2001)

	US	California
Number of Public Companies	342	129
Revenues	$25.3 Billion	>$13.5 Billion
R&D Expenditures	$11.5 Billion	>$5.4 Billion
Employment	141,000	>60,000

Sources: Ernst & Young (2002), California Healthcare Institute (2002), Burrill & Co. (2002), and UC IUCRP Economic Research and Assessment analysis

The findings of the biotechnology case study, described below, illustrate the essential role publicly funded research and education have played in the development of commercial biotechnology in California, which can be viewed as

the field's center of origin and a continuing source of economic growth and innovation.

The California Biotechnology Industry Case Study: A Brief History

The University of California Biotechnology Research and Education Program launched the California biotechnology industry case study in 1995, at a time when the US Congress was undertaking a highly skeptical review of public investments in scientific research and graduate education. Research universities, including the University of California, were challenged to provide tangible evidence of economic benefits accruing to academic research and graduate education. This charge posed a challenge to economists, as well, because of the difficulty in making strong economic claims based on the traditional academic research productivity measures of patents and publications.[xvi]

A number of qualitative studies show academic research is key to the development of many new products and processes.[xvii] Technology licenses have been the focus of numerous analyses about the economic value of scientific discoveries made in academic laboratories.[xviii] While companies' interest in holding UC technology licenses provides a quantifiable measure of the economic value of University research, to stop at licensing would be to miss much of the story. Studies of licensing data provide insight into the geographical patterns of technology diffusion over time, but licenses alone do not explain why so many biotechnology companies have chosen to locate in California, for example, nor why some of these firms have been so successful.

A series of studies by Lynne Zucker and Michael Darby of UCLA, and their colleagues,[xix] provides insight into this clustering phenomenon. They found that the biotechnology companies in their sample tend to locate near centers of research excellence, with regional clusters, for example, in New England near Harvard, MIT and Yale, and in California around University of California campuses and Stanford University. Business analysts have also found that proximity to world class research institutions, and the presence of an educated, highly skilled labor force are positively correlated with the productivity of local and regional private enterprises, and thus are magnets for business investment.[xx]

An analysis of the set of California biotechnology firms in this study (roughly twice as many California firms as in the 1994 study by Zucker et al, based on a broader definition of "biotechnology") confirms this pattern of geographical concentration. For the 2002 California biotechnology company cohort, 96% of public companies are located within 35 miles of a UC campus, and 58% percent are within 15 miles.

We have taken the view that publicly funded research and education is best viewed in the context of the broad range of contributions universities make to economic growth. In the spirit of Zucker et al,[xxi] and Audretsch and Stephan (1996), this study is focused on the activities of individuals. For biotechnology, these contributions include scientific leadership in founding or substantially contributing to the establishment and success of biotechnology firms; graduate education in the highly competitive and creative basic bioscience research environment, which prepares the highly skilled workforce needed to successfully develop, produce and market new biotechnology based products; and scientific innovation which produces discoveries that advance fields of inquiry into exciting and often unexpected directions, new research findings that form the substrate for licensing and future commercial trajectories, or fruitful early stage research collaborations with companies that create a confluence of research strengths from universities and industry to advance important new frontiers, such as genomics, or to establish proof of concept of nascent discoveries.

We wish to emphasize the preliminary nature of this study, noting that a great deal of work remains to be done. For example, it would be of interest to examine the effectiveness of alternative technology transfer policies, the relationship between local economic development efforts and geographically localized industry clusters, the value of graduate education to different strata of biotech firms, and the extent to which ongoing relationships with academic researchers contribute to business success.

Latest Findings (2002)

The University of California clearly continues to serve as a key driver on the commercial biotechnology economy

- **1** in **4** US public biotechnology firms is within 35 miles of a UC campus
- **1** in **6** U.S. public biotechnology firms was founded by UC scientists
- **1** in **3** California biotechnology firms was founded by UC scientists, including **5** of the world's **10** largest: Amgen, Genentech, Idec Pharmaceuticals, Applied Biosystems and Chiron[xxii]

In the following section, we examine separately the results in light of the four distinct avenues through which knowledge generators contribute to the biotechnology economy; scientific leadership, workforce, scientific research and technology transfer.

Scientific leadership

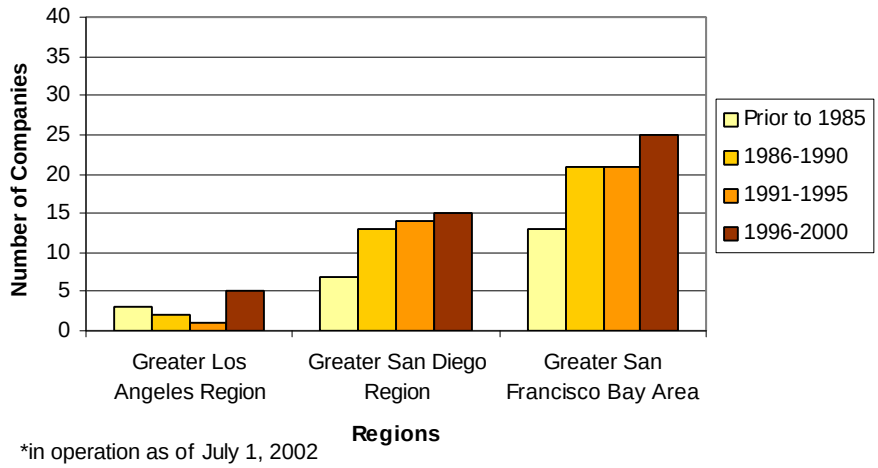
One of the most tangible ways that knowledge generators contribute to the emergence of new industries is through the founding of firms. Start-up activity by academic scientists has been the focus of intense interest by economists, including e.g., Zucker et al (1994, 1995), Audretsch and Stephan (1996) and others. Conceptually, there are two major categories of academic scientists who found biotech businesses. The first are those who have made a specific

discovery that has commercial potential. Generally, the development of a marketable process or product requires extensive research efforts that are highly applied in focus, and thus not within the usual bounds of academic research. University scientists may seek to license their discovery to an ongoing concern or, if no such firms are interested, if license terms are not satisfactory, or if the scientist is strongly committed to entrepreneurship, start up their own venture to take on these developments. A second category consists of scientists who recognize a commercial opportunity to which they can apply their expertise, which does not involve their tangible intellectual property that would be subject to a license. For the purposes of this study, in part for reasons cited in the section below regarding technology licenses, we do not distinguish between these two subgroups of founders.

2002 Scientific leadership update:
UC scientists are actively engaged in founding new biotechnology companies in California.[xxiii] Of the 402 companies in the 2002 California biotechnology cohort, at least 140, or 35%, were founded by UC faculty, graduates or postdoctoral fellows. This number is likely to be an underestimate, because many companies do not report the academic linkages of their founders, and in some cases companies do not identify their founders at all. Note that to maintain the integrity of the proportional estimates, this dataset includes only those biotechnology companies identified using a standard methodology that relies on public databases and directories. Details can be found in Appendix B.[xxiv]

The geographic distribution of start-up activity has remained quite consistent over time, and in every region, the number of firms founded by UC scientists increased for the period 1996-2000, compared to all previous 5-year intervals.

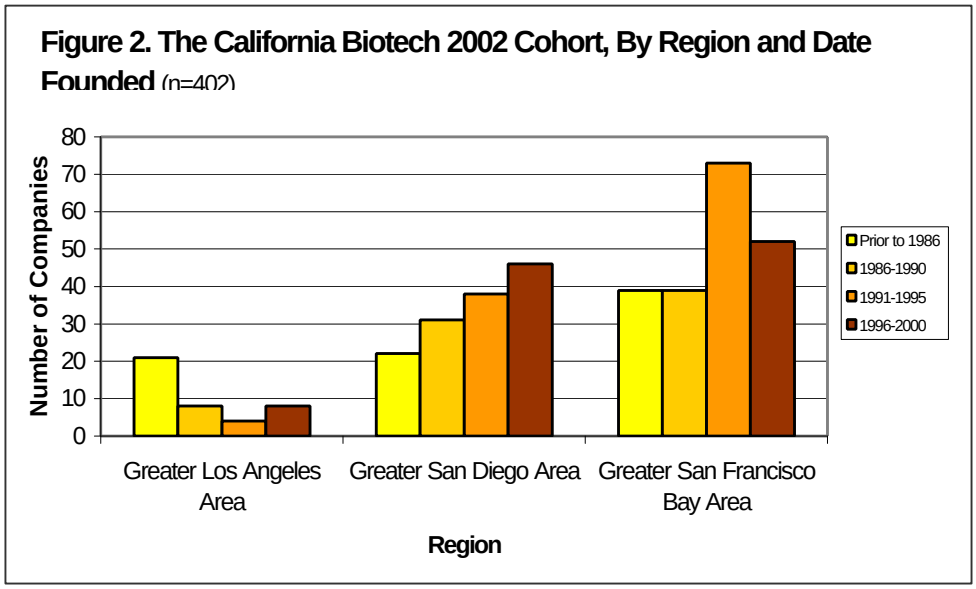
Figure 1. Regional Growth: Firms Founded By UC Scientists* (n=140)



*in operation as of July 1, 2002

As **Figure 1** illustrates, the strongest growth continues to be in the San Francisco Bay Area, followed by the San Diego area, largely in and around La Jolla, and, somewhat less so the Greater Los Angeles Area. It is interesting to compare this pattern of growth with the overall industry. As can be seen in **Figure 2**, the overall level of start-up activity increased in the San Diego and Los Angeles regions in the period 1996-2000, but slowed slightly in the

Greater San Francisco Bay Area. Thus, the proportion of UC founded companies in the San Francisco Bay Area is increasing strongly.



Another way to illustrate the impact of UC scientists on local biotechnology development is to consider the proportion of firms they have founded in the cities that have the largest concentration of biotechnology firms in the 2002 cohort. The city that is home to the largest number of biotech firms is San Diego, where 111 companies are located. Fully 33% of those firms were founded by UC scientists, as shown in **Table 2**. In northern California, South San Francisco is home to a burgeoning biotech business cluster of 31 firms, 48% of which were founded by UC scientists. Also impressive is the fact that UC scientists founded roughly half the firms in the cities of Hayward and Fremont, and 42% of those in Alameda.

Table 2. Top Ten California Cities With the Largest Number of Biotech Firms

City	Total Number of Biotech Firms	Firms with UC Founders	
		number	*percent*
San Diego	111	37	33%
South San Francisco	31	15	48%
Carlsbad	18	6	33%
Palo Alto	18	3	17%
Mountain View	13	2	15%
Alameda	12	5	42%
Hayward	11	6	55%
La Jolla	11	4	36%
Fremont	10	5	50%
Irvine	9	2	22%
Subtotal – Top 10 Cities	244	85	35%

Overall, it appears that the proportion of companies with UC founders is growing over time. In the initial cohort of 228 California biotechnology companies identified in 1995, 79 (34%) had UC founders. For the more recent period, 1996-2000, 106 new biotech firms were established in California, 45 (42%) of which were founded by UC scientists. This strong showing is of interest, because it confirms that the scientific leadership of UC faculty and graduates continues to be essential to the state's entrepreneurial biotechnology enterprise.

A second means by which academic scientists contribute leadership to biotech firms is through service on scientific advisory boards. For 43 (36%) of the 120 biotechnology companies that were founded in the 5-year period 1996-2000, company documents show that UC scientists are serving as scientific advisory board members. In all, we identified 84 UC scientists who are contributing their expertise to these young companies through membership on their Scientific Advisory Boards, including 61 UC faculty members. Two others are UC research scientists, one at a UC-managed national laboratory, and the other the director of a UC research center. The other 14 UC scientists in this group include people who earned their PhD at UC (9), were UC postdoctoral scholars (4), or earned a BS at UC (1) and are now faculty members elsewhere. In some cases, company founders also serve as members of a company's Scientific Advisory Board; this is the case for 22 of the UC scientists in this group, including 17 faculty members. An additional 3 UC scientists were identified who founded California biotechnology firms, but serve as Scientific Advisory Board members for companies they did not found.

Workforce

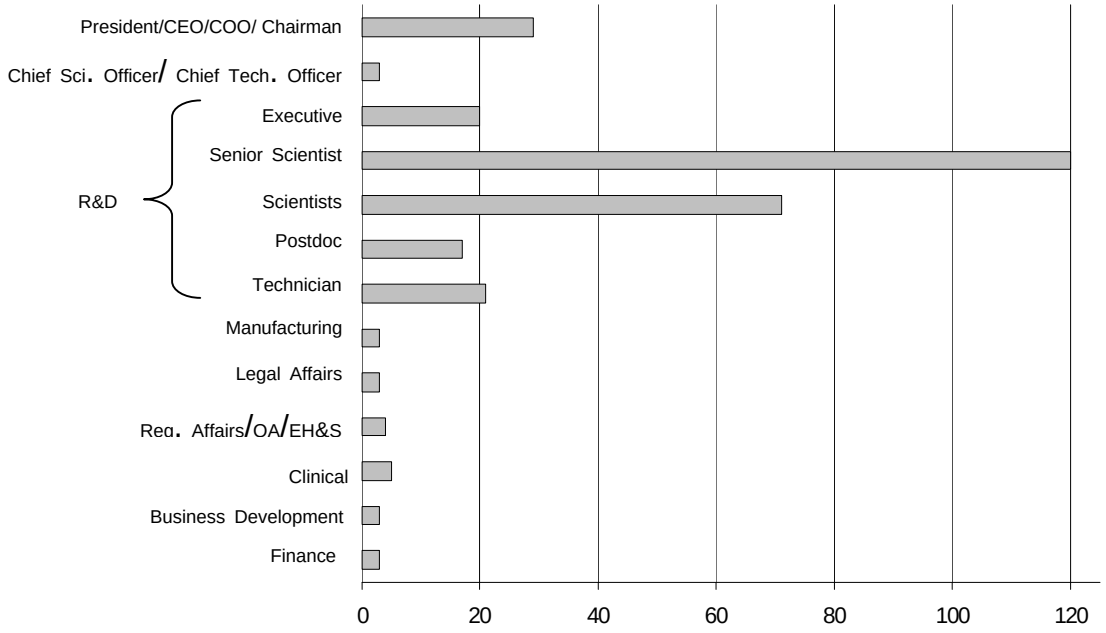
The availability of a highly skilled workforce is another key element contributing to the success of the commercial biotechnology enterprise in California. As noted in the background section, there exists a strong correlation between the location and vitality of high tech business activity and the presence of college and university graduates in the labor pool. The employment of UC alumni, particularly in senior scientific positions, allows skills acquired at the University to be applied to the development of innovative new products and processes, providing the basis for high paying jobs for the alumni themselves, their staff, and affiliated businesses.

Initial Workforce Findings:

The importance of UC in educating the biotech workforce is evident from the responses received to the Critical Linkages employment survey, promulgated in 1995-96. Responses were received from 134 firms, which constituted 58% of California biotechnology companies operating in 1995. Eighty-eight percent of those responding reported employing UC alumni, including 100% of respondents with more than 20 employees. Nearly as many firms, 85%, reported employing UC alumni with graduate degrees, which offers strong evidence for the importance of graduate education to the biotech economy in California.

Altogether 302 scientists with UC PhDs working in California biotechnology companies were identified from the survey responses. The strong contributions of UC PhD scientists to the executive ranks can be seen in **Figure 4**, which shows that most are senior scientists, but a substantial number are senior corporate leaders, as well.

Figure 4. Positions Held by UC PhDs (n=302)



It is notable that although the majority of these employees earned their doctorates at UC Berkeley, UC San Diego, UCLA or UC Davis, all nine UC campuses are represented, as can be seen in **Table 3**.

Table 3. Campus Source of PhDs employed by California biotech companies (1995)

Campus of Degree	**UC PhDs Employed by California Biotech Companies**	
	Number	*Percent*
UC, Berkeley	76	25
UC, San Diego	54	18
UC, Los Angeles	48	16
UC, Davis	45	15
UC, San Francisco	24	8
UC, Irvine	24	8
UC, Riverside	15	5
UC, Santa Cruz	9	3
UC, Santa Barbara	6	2

2002 Workforce Findings

In the latest update of the California biotechnology company cohort, we reviewed public company documents for information about UC scientists serving as executives. Companies generally list the names and biographies of just a few people in their corporate documents, suggesting that those listed are people

deemed most critical to the success of the business operations, and most likely to be of interest to investors. For R&D-intensive companies like those in this study, this group usually includes, in addition to the president and CEO, the vice president of R&D, and often the chief scientist, chief scientific officer, or other titles designating senior scientific research leadership.[xxv] Other key executive roles involve business development, legal affairs, clinical development, pharmaceutical manufacturing and financial affairs.

Data was available to characterize the academic background of key executives for 95 of the 120 new firms established in the period 1996-2000. UC scientists are playing leading executive roles at 60 of these new California biotechnology companies (63%). Graduate education and postdoctoral research continue to be directly relevant to these businesses; sixty-six of the 108 key executives with UC affiliations identified in this study have UC graduate degrees and/or postdoctoral experience. An additional 20 people are adjunct, emeritus or on-leave UC faculty members. These numbers certainly understate the importance of advanced academic research training to these companies, as they reflect only those key executives and scientists that they profile in their public documents. The many graduate-level scientists working in important, but less prominent roles, are much more difficult to identify.

Another way to view the important leadership role of UC scientists at these companies is to note the specific positions they hold. The largest group consists of Presidents and/or CEOs (27), followed by the group of Chief Scientific Officer/Chief Technical Officers (11 people). Seven UC scientists serve as Vice Presidents of Research and Development, and another five serve as Chief or Senior Scientists. Eleven are engaged in business development, and nine in legal affairs. A list of the specific job titles of UC alumni, postdoctoral scholars and faculty as reported by California biotechnology companies founded during the period 1996-2000 is listed in **Appendix C.**

Research in Science and Engineering

In addition to scientific leadership and education, economic benefits accrue to research conducted by UC faculty and Laboratory scientists, which generates discoveries that add value to California biotechnology firms. Given the complexity of cutting edge technologies, individual firms often lack the resources to assemble and staff research facilities that can address all obstacles encountered along in a particular research path; access to the expertise and facilities of University researchers working on fundamental or applied research is essential to the success of such projects.[xxvi] One indication of the importance of UC scientific innovation is the willingness of firms to support faculty and laboratory research projects.

2002 Research Findings:

Fifty eight California biotechnology companies sponsored over 172 research projects valued at more than $36 million at the University of California in the

period 1996-2000, excluding clinical trials. These research projects were distributed across all nine UC campuses, as can be seen in **Table 4**.

Table 4. California Biotechnology Companies' Research Sponsorship at the University of California 1996-2000

Campus	Number of Companies	Number of Research Awards	Dollar Value of Awards
Berkeley	14	17	1,679,321
Davis	9	15	1,426,943
Irvine	9	15	3,734,048
Los Angeles	11	30	2,425,880
Riverside	1	1	201,931
Santa Barbara	9	12	994,383
Santa Cruz	4	9	825,455
San Diego	29	63	13,694,573
San Francisco	28	50	11,034,428
Total	82	212	36,016,962

These statistics understate the level of research sponsorship by California biotechnology companies, in part because the data on research support at the University of California is complex, as the responsibility for negotiating research agreements with companies and other research sponsors, and recording the research awards is handled separately at each of the 9 campuses. A few descriptive pieces of data on each award are collected quarterly in the Contracts and Grants database managed by the UC Office of the President, Research Administration Office, which was the source for this data set. In addition to the variation in the completeness of reporting across campuses, another limitation of these data for the purposes of this study is that the awards are generally tracked at the level of the highest corporate parent. That means it is not possible to distinguish awards that are for research relationships between the California subsidiary of a major firm, and those projects sponsored by the non-California corporate headquarters. Because they could not be definitively linked to the California location, those records are excluded from the analysis. Nonetheless, even this very conservative set gives a view of strong research relationships between California biotechnology companies and UC faculty members.

Technology Licenses

Technology transfer activities create economic value by facilitating the translation of University research into tangible commercial products and processes. Licensing of the innovations developed by UC researchers allows firms to establish property rights to the technology, so that they can recoup the investment in applied research, product development, manufacturing, marketing and distribution required to successfully bring the innovation to market. While it can be argued that one indicator of the value of research conducted at UC to the biotechnology industry is the amount of money that firms pay the University to license UC technology, this indicator is subject to several important limitations. Technologies licensed by universities arise from discovery research, and may require substantial additional investments in applied research and development by the licensee before a marketable product is developed. Further, licensing

revenues are typically linked to the sales of a product, so revenues do not accrue until after a product has been commercialized, which may take many years. Despite the measurement issues, licensing remains an important channel for technology transfer.[xxvii]

Technology Licensing Findings:
One of the academic inventions that had broad impact on the emergence of commercial biotechnology was the "Process for Gene Splicing," more commonly known as the Cohen-Boyer patent, after inventors Stanley Cohen of Stanford University and Herbert Boyer of UCSF. It is estimated to have generated more than $170 million in licensing revenues for the two institutions over the 20-year life of the patent.[xxviii] This fundamental biotechnology invention, which went off patent in 1997, was widely licensed by companies across the nation and the world. For the purposes of this study we looked only at California biotechnology companies. In 1995, 82 of these companies held active licenses for UC technology. Seventy licensed the Cohen-Boyer patent, 32 held other UC licenses, and 20 companies held both types of licenses.[xxix]

The relative importance to a company of any given license is a question worthy of further research. Although not systematically examined, it is clear from the company documents reviewed for this study that many biotechnology businesses hold multiple licenses from a diverse array of academic institutions, research institutes and other businesses. Indeed, a major means of realizing value for many biotech companies is the licensing of technology to other firms. A systematic study of the role of licensing in business development, and the role of academic licenses in overall intellectual property portfolios would be a useful line of future research.

Conclusions

The major hypothesis underlying the Industry-University Cooperative Research Program Economic Assessment Initiative is that people, particularly those whom we have termed "knowledge generators," are the drivers on today's knowledge-based economy. To provide a concrete foundation for assessing the contributions of knowledge generators, we developed a framework in which we identified a comprehensive set of "core" biotechnology companies in California, then systematically undertook to identify and document the roles that University of California faculty and alumni have played, and continue to play at these firms. This approach contrasts with that taken by most economic studies of the contribution of research and education to the economy, which generally have focused on a small set of indicators, especially publishing, patenting, and relative citation rates. While most such studies conclude that public investments in basic research and graduate training generate substantial economic benefits, they do not have a means to explain just what happens between the academic activities and the economic outcomes, leaving the process as a "black box." We have shown a light into this area, providing a unique, close-up view of that translation

process. The University of California biotechnology case study clearly demonstrates that university faculty and alumni contribute to commercial biotechnology through a variety of channels, including starting up firms, serving as scientific advisors and key R&D personnel, conducting sponsored research and producing discoveries that are licensed by firms.

This study has examined a single sector of the economy, biotechnology, and looked solely at activities occurring in just one state, California, focusing on those relating to the public research university system. An important question for future research is whether the pattern of contributions by knowledge generators that we identified in this study can be generalized. Similar case studies are under development in other high technology sectors, including communications, and electronics manufacturing. A study that examines one or more of the several other US or international biotechnology clusters would provide a means to assess whether the centrality of knowledge generators to the development of commercial biotechnology that we find in California generalizes. The data collection effort undertaken for this study was substantial; if this framework is to be useful in a larger context, efforts will have to be made to find effective ways to streamline and simplify reporting of relevant information. Finally, we have just scratched the surface in asking questions of the dataset for this case study. Many important questions remain to be investigated, including questions about relative performance of faculty-founded companies, variation in patterns of relationships (licensing, contract research, alumni employment) in faculty-founded versus other companies, and the impact on faculty members academic career paths of relationships with companies.

Acknowledgments:

The following people and organizations provided valuable contributions to this study: Prof. Lynne Zucker, Institute for Social Science Research, UCLA; Prof. Michael Darby, Anderson School of Management, UCLA, UC Systemwide Biotechnology Research and Education Program Executive Committee members, Prof. Suresh Subramani, Dept. of Biology, UCSD; Dr. Greg Lennon, Lawrence Livermore National Laboratory; Dr. Paul Jackson, Los Alamos National Laboratory; Barbara Yoder, Lynn Judnich, Suzanne Quick and Joe Acanfora, UC Office of Technology Transfer. Alameda; Delia Talamantez, UCSD Conflict of Interest Office; David Gilbert, Vivianna Wolinksi, and Jeff Weiner, Lawrence Berkeley National Laboratory; John Mott, Los Alamos National Laboratory; Mark Edwards and Satomi Degami, Recombinant Capital, San Francisco; Bill Otterson and Dr. Abi Barrow, UCSD CONNECT; Doug Windsor and Jean Cunicelli, Ernst and Young, Palo Alto; Jeannine Niacaris, Bay Area Personnel People in the Life Sciences; William Hoskins, UC Berkeley Office of Technology Licensing; John Tucker, UCSF; and the alumni associations and related University offices at all nine campuses. The research assistance of Andrew Murray, Patrick Wang, Alexander Gomozias, and Lisa Gurley has been essential. None of the analysis reported here would have been possible without the database design advice and mentorship of Prof. Michael Cooper, UC Berkeley School of Information Management.

I indebted to Fred Gault, Paula Stephan, David Mowery and the participants at the Statistics Canada/PRIME Advanced Research Workshop on the Economic and Social Dynamics of Biotechnology (Ottawa, February 24, 2000), and the University of California IUCPR Economic Indicators for Academic Science Workshop (Berkeley, March 2000) for their comments and suggestions. This study was funded by the University of California Biotechnology Research and Education Program, and subsequently the Industry-University Cooperative Research Program. Susanne Huttner, director of both programs, has been instrumental in providing support and direction for the project.

References

Arundel, A. and A. Rose, 1999. "The diffusion of environmental biotechnology in Canada: adoption strategies and cost offsets." *Technovation* 19, 551-560.

Audretsch, D. and P. Stephan. 1996. "Company-scientist locational links: the case of biotechnology." *American Economic Review* 86(3): 641-653.

Eliasson, G. and A. Eliasson, 1996. "The Biotechnological Competence Bloc." *Revue D'Economie Industrielle* 78(4): 7-26.

Ernst & Young Global Health Sciences 2002. "Beyond Borders: The Global Biotechnology Report 2002." Ernst & Young LLP. United Kingdom.

Griliches, Z., 1990. "Patent Statistics as Economic Indicators: A Survey." Journal of Economic Literature. 28(3): 1661-1707.

Griliches, Z. 1992. "The Search for R&D Spillovers", *Scandinavian Journal Of Economics, 94 Supplement*: 29-47.

Griliches, Z. 1994. "Productivity, R&D, and the Data Constraint", *American Economic Review* 84:1-22

Henderson, R., A. Jaffe, and M. Trajtenberg, 1998, "Universities as a Source of Commercial Technology: A Detailed Analysis of University Patenting, 1965-1988." *Review of Economics and Statistics* 119-127.

Intersociety Working Group, American Association for the Advancement of Science. 2000. "AAAS Report XXVI Research and Development FY 2000." Washington DC.

Lee, K. and G. S. Burrill. 1996. "Biotech 97 Alignment: The Eleventh Industry Annual Report." Ernst and Young LLP. Palo Alto, CA.

Link, A. 1999. "A Suggested Method for Assessing the Economic Impacts of University R&D: Including Identifying Roles for Technology Transfer Officers." *Journal of the Association of University Technology Managers*. XI.

Mansfield, E., 1994. "Academic Research Underlying Industrial Innovations: Sources, Characteristics and Financing." *Review of Economics and Statistics*. 77: 55-62.

Pisano, G. 1988. "Innovation through markets, hierarchies, and joint ventures: Technology strategy and collaborative arrangements in the biotechnology industry," Doctoral dissertation, UC Berkeley

University of California Technology Transfer Program. 2002. UC Technology Transfer Annual Report 2001. University of California Office of the President. Oakland, CA.

Zucker, L., M. Darby and M. Brewer. 1994 "Intellectual Human Capital and the Birth of U.S. Biotechnology Enterprises." Working Paper No. 4653 (Feb.) Cambridge, MA. National Bureau of Economic Research.

Zucker, L., M. Darby and J. Armstrong. 1996 "Geographically Localized Knowledge: Spillovers or Markets?" *Economic Inquiry* 36(1): 65-86.

Zucker, L., M. Darby and M. Brewer. 1998 "Intellectual Human Capital and the Birth of U.S. Biotechnology Enterprises." American Economic Review 88(1): 290-306

Appendix A: Critical Linkages Project employment survey form (attachment)

Appendix B. Methodology

The initial assessment of commercial biotechnology activity in California required that we define 'biotechnology' and determine which business entities constituted the appropriate target of study. For the purposes of this study we focus on the subset of firms for which biotechnology is a primary activity.[xxx] We adopt the definitions of 'new biotechnology enterprises' introduced by Zucker, Darby and Brewer (1994).[xxxi] Our definition is consistent with that found in Eliasson (1996), and includes recombinant DNA technology, the use of antibodies (often termed cell fusion), and protein engineering.[xxxii] For the purposes of this study, a 'core' biotechnology company is one in which the tools of molecular biology are used in research, development and, where applicable, production of a product. We count separately each business establishment that (a) has a recognizable, separable identity, and (b) undertakes biotechnology-based R&D activity. Following Zucker, Darby and Brewer (1994), this definition includes both start-up companies (what they term 'new biotechnology enterprises') and subunits of existing firms (their 'new biotech subunits').

These definitions had important implications for data collection. Major sources of economic data are the databases maintained by government agencies, such as the US Patent and Trademark Office and the Bureau of the Census, and proprietary databases of patent citations and journal articles. These sources were unsuitable for the initial definition of the population of biotechnology companies in the State for several reasons. Government databases, and many proprietary information services, categorize and report data using standard industrial classification (SIC) codes. These codes use a hierarchical system of increasing specificity to define industry sectors and organize data. For new technologies and emerging industries, the SIC codes do not reflect the categories that actually define the industry. For example, some biotechnology companies that develop therapeutics are categorized under SIC code 2834, Pharmaceutical Preparations, along with many companies that use standard biochemistry. Other biotechnology companies are classified under SIC code 2836, Biological Products, but companies that simply produce plasma and serums are also categorized under this code. A number of organizations that report on biotechnology activity, such as the California Healthcare Institute, do not separate biotechnology companies from biomedical companies, while others rely on company self-reporting instead of a particular definition. Therefore, in order to construct a complete, well-defined dataset, we used a multi-step approach.

Firms were identified using industry directories, and through consultation with experts at the University and in the private sector. The initial list of "core" companies was developed by undertaking a systematic review of the following biotechnology industry directories: *BIOSCAN Directory of Biotech Companies* (1994 and 1995); *Coombs Biotechnology Directory* (1995); *Standard and Poor's Corporation Register of Directors and Executives* (1995); *The Bioscience Directory, San Diego County Edition* (1995); and *California Biotechnology Corporate Directory* (1995). The initial list was vetted with a broad range of experts, including a biotechnology analyst at Ernst and Young LLP; Mark

Edwards, Managing Director of Recombinant Capital, a San Francisco-based consulting firm specializing in biotechnology alliances and capitalization; the 12 UC Biotechnology Research and Education Program Executive and Advisory Committee members; several other UC faculty members who were also company founders; UC campus alumni association and development offices; and UC patent coordinators.

Approximately 400 California companies were assessed for inclusion in the database. By applying a definition of 'biotechnology' that emphasizes the use of modern molecular techniques, and after accounting for firms that had merged, moved out of state or gone out of business, the list was narrowed to 228 firms. It should be noted that because the number of California biotechnology companies is continually changing, the CLP "core" list is regularly updated to reflect the most current available information. Although this paper reports only our initial findings from the original data set, the database is structured to track information about each company over time, so that UC contributions can be traced as the industry evolves.

Once the dataset was constructed, we assessed the opportunities to use existing databases, such as those maintained by federal, state and local agencies with responsibilities to track business data (e.g., business licenses, payroll). These databases for the most part did not contain the data elements of interest to this study. For example, company business licenses name corporate officers, but not necessarily founders, and contain no biographical data. We next turned to University resources. The contracts and grants data, and some of that relating to technology licenses, was relatively straightforward to access and incorporate. The data about the people, however, was not. Alumni associations keep lists of their members, but employment data is self-reported, often outdated, incomplete and generally not reliable enough for this purpose. Similarly, academic departments rarely maintain systematic collections of this kind of information.

Data collection: Founders

Information about company founders was derived from a systematic review of available corporate documents, including corporate profiles, prospectes, California Department of Corporations filings, and 10-K forms. Data recorded includes the names and affiliations of both UC and non-UC founders. Information about private biotechnology companies is relatively difficult to find, and in general the names and UC affiliations, if any, of company founders are not readily available. Mark Edwards, Managing Director of the Recombinant Capital, generously provided access to his extensive collection of biotechnology company information, including corporate profiles, filings with the California Department of Corporations, and corporate prospectes. Bill Otterson, Director of UCSD CONNECT graciously allowed CLP researchers to review the entire set of corporate profiles in the CONNECT archives, from which a number of UC linkages were identified.

To compile a systematic set of corporate information, a post card was sent to all "core" companies requesting that the Critical Linkages Project be placed on

the corporate mailing list. The response rate for public companies was 100%, but the response rate for private companies was less than 25%, reflecting differences in legal reporting requirements and information dissemination strategies across the two groups. The information provided by public companies includes Security and Exchange Commission 10K reports, prospectes, corporate profiles, and in some cases stock analysts' reports and press releases. For private companies, the information provided is generally limited to corporate profiles, occasional press releases and product catalogs. Advances in electronic databases and World Wide Web-based resources have allowed, since 1997, access to most information about public companies on-line.

Data collection: Workforce

The absence of reliable alumni employment information from University or private sources convinced us that a direct survey of companies would be necessary. We created a simple survey instrument, consisting of a table with row headings, "Job Title," "Name," "UC Campus Attended," "Degree" and "Year." A copy can be found in Appendix A. Every "core" company was then contacted. First, a telephone call was made to the human resource director (or the equivalent) to introduce the Critical Linkages Project and to solicit preliminary information and a commitment to participate. All companies were given complete assurances that the data they provided would be held in strict confidence. Then, for companies agreeing to participate, a printed survey form was sent to the attention of the appropriate information source at the firm, generally the director of human resources. If completed survey forms were not returned within 3 weeks, follow-up telephone calls were made to encourage participation. For those who did not fill out the survey form, but did supply information by phone about UC alumni employment, letters were sent out requesting written confirmation of the information provided. Only information received from companies in written form was entered into the database.

Approximately 58% of companies surveyed (136 out of 228 companies) provided partial or complete responses to the survey. Eighteen firms declined to participate. Forty-four firms expressed initial interest but did not return survey forms. For the remaining 31 firms, the person responsible for human resource information could not be reached by phone.

Data collection: Contract and Grants and Technology Transfer

In contrast to the foregoing categories of information, the University undertakes extensive tracking of contracts and grants and technology transfer activities, albeit with certain limitations. Information about contracts and grants funded by California biotechnology companies was provided by the UC Contracts and Grants Office. The set of research contracts funded by "core" firms was constructed by matching the CLP "core" list to the set of information on all research contracts in the UC Contracts and Grants database for the fiscal year 1994-95. The Phase I findings reflect grant activities reported in FY 94-95 only, although the Critical Linkages database will be updated to include data reflecting subsequent years. A major Project initiative currently underway seeks to

reconcile the manner in which business entities, such as those included in this study, are tracked in the various UC databases with relevant data. For the initial work, a comprehensive manual review of all records involving private company sponsors of UC research in the Contracts and Grants database was undertaken to assure an exhaustive mapping between the two data sets.

Technology license information was provided by the UC Office of Technology Transfer for the licenses under their purview. Due to legal constraints on disclosure, information about individual licenses was not provided, but rather a count was made by comparing the CLP "core" list to the OTT list of licensees. Information about technology licenses from the UC-managed National Laboratories was collected via a phone survey of the technology transfer and industrial partnership offices at Lawrence Berkeley National Laboratory, Lawrence Livermore National Laboratory and Los Alamos National Laboratory. Data from the autonomous technology transfer offices at UC Berkeley, UC San Diego and UCLA remains to be collected.

Data Sources for the Summer 2002 Update

The update process includes annual review of directories and membership lists to identify new companies that fit the definition of California biotechnology firm; that is, for profit entities that use the tools of modern molecular biology and maintain active R&D activities in the state. Once an exhaustive search has been completed for new firms, data is collected to characterize the firms by location, number of employees, and the academic background of founders and executives. The following resources are used for these purposes:

California Healthcare Institute Biomedical Resource Online Directory of California Biomedical Companies (www.chi.org/ biomedicalresource.php)

Knowledge Express (CorpTech and BioSCAN directories, accessed through the University of California site license portal, http://members.knowledgeexpress.com)

Hoovers Online Directory (www.hoovers.com)

PriceWaterhouseCoopers Moneytree Venture Capital Survey (www.pwcmoneytree.com)

Yahoo– Biotechnology Industry News (http://biz.yahoo.com/news/biotechnology.html)

California biotechnology company web pages (various)

TechVentures Network, fka. Bay Area Regional Technology Alliance (www.techventuresnetwork.org/)

Los Angeles Regional Technology Alliance (www.larta.org)

San Diego Regional Technology Alliance (www.sdrta.org)

---

i An earlier version of this paper was presented to the Statistics Canada/PRIME Advanced Research Workshop on the Economic and Social Dynamics of Biotechnology Workshop Feb. 24-

25, 2000 Ottawa, Ontario Canada. That paper reported on the 1996 study; this paper reports on the second phase of the study, which re-examines the California biotechnology industry in 2002.

[ii] Porter, M. "Clusters of Innovation: Regional Foundations of U.S. Competitiveness." Council on Competitiveness. Washington, D.C. 2001, Tornatzky L.G, Waugaman P.G., and D.O. Gray. "Innovation U: New University Roles in a Knowledge Economy." Southern Growth Policies Board. Research Triangle Park. 2002. Accessed on line 9/3/2002. http://www.southern.org/pubs/stc/innovationU/, and others.

[iii] One underlying issue is the data constraint; that is, data collection is expensive so analysts frequently rely on the data that government agencies have collected for other purposes. The level of aggregation, definition of technologies or industrial sectors, and range of variables for which data is available often preclude direct analysis of the phenomena of interest. See, e.g., Griliches (1994).

[iv] Ernst and Young. "Focus on Fundamentals: The Biotechnology Report, Ernst & Young's 15th Annual Review." 2001.

[v] California Healthcare Institute and PricewaterhouseCoopers. Biomedicine: The Next Wave for California's Economy. January 31, 2002. Figure represents average wages in biopharmaceuticals, from chart on page 15.

[vi] Burrill & Company LLC. "Biotech 2002: The 16th annual report on the industry." San Francisco. 2002.

[vii] Based on total market capitalization as of December 31, 2001. From Burrill & Company LLC. "Biotech 2002: The 16th annual report on the industry." San Francisco. 2002.

[viii] Intersociety Working Group, American Association for the Advancement of Science (1999). Table I-14shows colleges and universities conducted 9.2% of total US R&D by dollar value in 1970, and 11.4% in 2000. Federal R&D went from 15.8% to 7.2% during the same period. Industry R&D rose from 67% in 1970 to 74.6% in 2000.

[ix] Mansfield surveyed R&D executives from 66 firms in seven industries. He found that recent academic research was cited as key to the development of 27% of new pharmaceutical products introduced from 1975-1985 (Mansfield 1994). His survey results show that researchers cited by firms for the importance of their discoveries typically receive both private and public funds for their research, with public funds outweighing those from industry by a factor of 3.

[x] One underlying issue is the data constraint; that is, data collection is expensive so analysts frequently rely on the data that government agencies have collected for other purposes. The level of aggregation, definition of technologies or industrial sectors, and range of variables for which data is available often preclude direct analysis of the phenomena of interest. See, e.g., Griliches (1994).

xi UC Office of Technology Transfer, "Income from Royalties and Fees by Technology Classification," 1996. An additional 250 Cohen-Boyer licensees are located outside the State according to Suzanne Quick of the Office of Technology Transfer.

xii E.g., Puzzanghera, J., "Biotech Companies Stay Close to Stanford," San Jose Mercury News, May 5, 1997

xiii Some faculty salaries and instructional services are supported by endowments or other funding sources.

xiv California Healthcare Institute and PricewaterhouseCoopers. Biomedicine: The Next Wave for California's Economy. January 31, 2002. Figure represents average wages in biopharmaceuticals, from chart on page 15.

[xv] See, e.g., Burrill & Company LLC. "Biotech 99 Life Sciences into the Millennium: The Biotechnology Industry Annual Report." San Francisco. 1999.

[xvi] For an excellent discussion of issues relating to the use of patents as economic indicators, see Griliches (1990, 1992).

[xvii] Mansfield, E., "Academic Research Underlying Industrial Innovations: Sources, Characteristics and Financing." *Rev. Econ. Stat*. 77 (1994): 55-62. Mansfield surveyed R&D executives from 66 firms in seven industries. He found that recent academic research was cited as key to the development of 27% of new pharmaceutical products introduced from 1975-1985 (Mansfield 1994). His survey results show that researchers cited by firms for the importance of their discoveries typically receive both private and public funds for their research, with public funds

outweighing those from industry by a factor of 3.

[xviii] Henderson, R., A. Jaffe, and M. Trajtenberg (1998); Link (1999)

[xix] Zucker, L.G., Darby, M.R., and Brewer, M.B., "Intellectual Capital and the Birth of U.S. Biotechnology Enterprises," Working Paper, Institute for Social Science Research, UCLA 1995

[xx] Barlyn, Suzanne, "It's San Francisco! [Best Cities for Business]", Fortune 132:10 November 13,1995; 84 (7 pages)

[xxi] See e.g., Zucker, Darby and Brewer (1994), Zucker, Darby and Armstrong (1996), Zucker, Darby and Brewer (1998)

[xxii] Based on total market capitalization as of December 31, 2001. From Burrill & Company LLC. "Biotech 2002: The 16th annual report on the industry." San Francisco. 2002.

[xxiii] This category consists of those who are designated "founder" or "co-founder" in company documents or official statements. It has been argued that this designation properly should be extended to initial scientific advisors, for example, or others whose expertise was crucial to successful establishment of the firm. A broader interpretation would likely increase the number of firms for which UC scientists could be considered founders; this issue will be taken up more exhaustively in later work.

[xxiv] Data on new companies was not collected from UC campus sources, such as technology licensing offices, because doing so might lead to over-representation of UC in the results.

[xxv] Corporate Board members who were not officers of the corporation were not included, as their focus is primarily the financial operations of the firm. The specific role of corporate boards in the governance of R&D intensive businesses may be an interesting topic for future research.

[xxvi] See Pisano (1988) for a study of the role of strategic alliances between established firms and biotech start-ups, based on a similar line of argument.

[xxvii] For example, The University of California Technology Transfer Program Annual Report 2001 reports 1,242 active licenses for fiscal year 2001, with 850 technologies generating royalties.

[xxviii] Hamilton, J. "Stanford's DNA patent 'enforcer' Grolle closes the $200M book on Cohen-Boyer." Signals Magazine. 11/25/1997.

[xxix] Based on a review of the California Biotechnology cohort for 1995 by Lynne Judnick, analyst for the University of California Office of Technology Transfer, May 22, 1996.

[xxx] An alternative approach, utilized by Arundel and Rose (1999), among others, recognizes that biotechnology is a set of techniques, rather than an industry sector akin to e.g., pharmaceuticals or agrochemicals. An interesting extension of this study would be to create a dataset of companies utilizing biotechnology anywhere in their operations. This approach would produce a larger, more diverse set of target companies, but create complexity in biotech-specific data collection.

[xxxi] In their 1994 study, Zucker et al focus on the use of recombinant DNA technology for the development of human therapeutics, a subset of the activities we include in this study.

[xxxii] Eliasson (1996) notes that the definition of biotechnology is empirically based, and "dependent on particular… techniques that constantly change." (pp. 13)

Appendix C. Executive Positions of UC Alumni, Postdoctoral Scholars and Adjunct, Emeritus and former Faculty At Young California Biotechnology Companies†.

Executive Position	Number of UC People
President, Chief Executive Officer	27
Chief Scientific Officer, Chief Technical Officer	11
Chief Financial Officer, Chief Business Officer, Chief Operating Officer	7
Vice President, Research & Development	7
Chief/Senior Scientist	5
President, Genetics Division	1
Senior Vice President, Drug Development	1
Senior Vice President, Bioinformatics	1
Vice President, Scientific Affairs	1
Vice President, Genomics	1
Vice President, Cell Biology	1
Vice President, Chemical Biology	1
Vice President, Discovery	1
Vice President, Informatics	1
Vice President, Pharmaceutical Product Development	1
Director of Chemistry	2
Director of Research & Development	2
Director, Microarray Automation	1
Director Informatics	1
Scientific Director	1
Senior Research Scientist	1
Scientific Investigator	1
Director of Cell Biology	1
Director of Molecular Biology	1
Principal Research Scientist/Principal Scientist	1
Molecular Biologist	2
Research Associate	1
Chemist	1
Senior Vice President, Business Development	1
Vice President, Business Development	4
Vice President, Scientific Partnering	1
Executive Director, Business Development	1
Director of Business Development	1
Director of Corporate Development	1
Associate Director, Business Development	1
Director of Marketing	1
Vice President, Clinical Development	3
Vice President, Preclinical Development	2
Vice President, Product Development	2
Senior Director of Pharmacology/Toxicology	1
Director of Clinical Research	1
Senior Director, Clinical Research	1
Medical Chemist	1
General Counsel	2
Vice President, Intellectual Property	2
Vice President, Operations	2
Senior Director of Intellectual Property	1
Director of Legal Affairs	1
Vice President and Chief Legal Counsel	1
Vice President, Quality Assurance	1
Vice President, Manufacturing	1
Director, Quality Assurance	
Senior Vice President, Operations	1
Vice President, Technology	1
Vice President, Information Sciences	1
Vice President, Engineering	1
Vice President, Finance and Administration	1
Vice President, Human Resources	1

†Source: Analysis of company documents